**REMARKS**

Claims 1-3, 5, 7, 10 and 12-17 presently appear in this case. No claims have been allowed. The official action of November 15, 2006, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to a method of detecting in a subject a proliferative-related disease state that is a tumor, or for determining the severity of such a disease state, or for determining whether a patient having such a disease state has a high probability of responding to a therapeutic treatment involving the administration of an A3AR agonist or antagonist. Cells suspected of being in the disease state are tested to detect the level of expression of A3AR as compared to that in control cells indicative of a normal state. This difference in levels is indicative of the disease state and is correlated to the severity of disease state, and is further indicative that the subject has a high probability of responding to a therapeutic treatment by an A3AR agonist or antagonist.

Claims 1-3, 7, 8, 12, 13, 16 and 17 have been rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting a tumor in a subject, a method for determining the severity of a tumor in a subject, and a method for determining whether a subject has a high probability of responding to a therapeutic treatment of tumor does not reasonably provide enablement for

a method of detecting any and all disease states in a subject including psoriasis. The examiner also states that the A3AR protein fragment recited in claims 12 and 13 are not supported by an enabling disclosure.

The claims have now been amended to be directed only to the subject matter that the examiner concedes as enabled, i.e., that relating to tumors. Reference to the treatment of psoriasis has now been deleted from the claims without prejudice toward the continuation of prosecution thereof in a continuing application. Furthermore, claims 12 and 13 have been amended to delete reference to fragments. Accordingly, this rejection has now been obviated.

Claims 1-5, 7-10, 12, 13 and 16-18 remain rejected under 35 U.S.C. 103(a), as being unpatentable over Baraldi in view of Reeves, Wei and Keyomarsi. The examiner states that Baraldi claims a method for determining the presence of tumor cells that possess a high concentration of adenosine A3 receptors in a patient or in a cell sample by administering a compound that includes a radiolabel or fluorescent label that can be detected following binding of the compound to tumor cells, followed by detection of the radiolabel. The examiner concedes that Baraldi does not expressly teach comparing the expression of A3AR in tumor cells to that in normal cells, but the examiner states that the method inherently comprises a step of comparing the expression of A3AR in tumor cells to that in normal cells or surrounding tissues in order to detect and differentiate the labeled tumor cells or residual tumor

cells from the surrounding cells or tissue. The examiner states that Baraldi's teachings about other functions of the A3AR do not indicate that A3AR is not differentially expressed in cancer cells versus normal cells and that A3AR could not be useful for cancer detection. The examiner further acknowledges that Baraldi does not teach comparing the level of the expression of A3AR to the values of a calibration curve, but the examiner states that this would be made obvious by Wei, who teach a method of determining the amount of the protein present in a given volume of a patient's sample by comparing against a standard curve. Thus, the examiner considers it to have been *prima facie* obvious to measure the level of expression of A3AR protein and thereafter detect a tumor or determine the severity of a tumor by comparing the level of expression of A3AR protein to a normal control tissue or to a standard curve in view of the teaching of Baraldi, Reeves, Wei and Keyomarsi. This rejection is respectfully traversed.

The present invention is based on the surprising finding that in cancer cells there is an increase in the level of A3 adenosine receptor expression as compared to non-cancerous cells obtained, for example, from the same subject from which the cancer cells were obtained (see page 2, lines 17-20 of the present specification). The examiner refers to what Baraldi teaches in its claimed methods. However, these claimed methods are not for determining the presence of tumor cells, they are for determining the presence of tumor cells

that possess a high concentration of adenosine A3 receptors. Certainly, if such cells light up, this establishes that those cells have a high concentration of A3AR. Such claims are based only on experiments relating to tumor cell lines (see example 18, column 38, lines 44-45 and column 39, lines 15-18 and 35-36). The fact that some human cell lines have high concentrations of A3AR does not establish that a natural human tumor will have a higher level of A3AR expression than control cells from the same patient. The experiments in the present specification were carried out on normal human cancer biopsy cells and normal cells. It is well known that results obtained from cell lines are often not relevant for natural cells. Accordingly, those of ordinary skill in art would not find it obvious from Baraldi that the method of the present invention would be feasible. As Reeves, Wei and Keyomarsi have nothing to do with A3AR receptors. They add nothing to the deficiencies of Baraldi in this regard.

Furthermore, the fact that tumor cells having high levels of A3AR can be detected by a radiolabeled compound that binds to A3AR does not make obvious present claim 7, which is directed to a method for determining the severity of a tumor disease state. There is nothing in Baraldi that would suggest that the higher the amount of A3AR the more severe is the disease state. There is nothing in the secondary references that would make this obvious. All Baraldi teaches is that tumor cells with high A3AR expression can be detected using a radiolabeled A3AR binder. The fact that the level of A3AR

expression can be correlated to the degree of severity of the disease state, something to which Baraldi is completely silent, is not made obvious by the disclosure of Baraldi, either alone or in combination with any of the other references of record.

Furthermore, claim 16 is not made obvious by Baraldi because Baraldi says nothing about whether or not a tumor having high A3 level expression is more or less likely to be treatable by an A3AR agonist or antagonist. Accordingly, claim 16 is also independently patentable over Baraldi. The secondary references teach nothing that would fulfill the deficiencies of Baraldi with respect to the method of determining whether a specific tumor has a high probability of responding to therapeutic treatment by administration of an A3AR agonist or antagonist.

For all of these reasons, the present claims are not made obvious by Baraldi alone or in combination with any of the other references of record. Reconsideration and withdrawal of this rejection is therefore respectfully urged.

It is submitted that all the claims now present in the case clearly define over the references of record and fully comply with 35 U.S.C. 112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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